Claims

1 An acid sensitive cation channel protein which is a SPASIC protein comprising amino acid sequence Seq ID No 2.

2 A SPASIC variant protein which
(i) has ion channel activity, and
(ii) comprises an amino acid sequence having at least 80% sequence identity with the full length sequence shown in Seq ID No 2.

3 A SPASIC variant protein as claimed in claim 2 which is a fragment of the SPASIC protein of claim 1.

4 A SPASIC variant protein as claimed in claim 2 which is capable of reversibly mediating (i) a rapid, and (ii) a sustained cation current.

5 An isolated nucleic acid comprising a polynucleotide sequence encoding the protein of ~~any one of the preceding claims~~ claim 1 or 2.

6 A nucleic acid as claimed in claim 5 wherein the polynucleotide sequence comprises bases 292-1909 of Seq ID No 1 or is degeneratively equivalent thereto.

7 A nucleic acid as claimed in claim 5 which encodes the SPASIC variant of claim 3.

8 A nucleic as claimed in claim 7 which is capable of hybridising with the complement of the nucleic acid of claim 6 under high stringency conditions, being 0.1 x SSC, 0.5% SDS at 68°C.

9 A nucleic acid as claimed in claim 7 or claim 8 which is an allelic variant.

10 A nucleic acid which is the complement of the nucleic acid of ~~any one of~~ claims 5 ~~to 9~~.

11 A nucleic acid molecule for use as a probe, which molecule comprises a contiguous polynucleotide sequence of at least 30, 50 or 100 bases found in Seq ID No 1, or a sequence degeneratively equivalent thereto, or the complement of either.

12 A nucleic acid molecule for use as a primer, which molecule comprises a contiguous polynucleotide sequence of at least 16, 18, 21 or 24 bases found in Seq ID No 1, or a sequence degeneratively equivalent thereto, or the complement of either.

13 A nucleic acid molecule as claimed in claim 12 wherein the contiguous polynucleotide sequence is one which is highly conserved between SPASIC and one or more other ion channel proteins selected from: DRASIC ;α-ASIC ; β-ASIC.

14 A nucleic acid molecule as claimed in claim 12 wherein the contiguous polynucleotide sequence is one which is not present in any of DRASIC ;α-ASIC ; β-ASIC.

15 A nucleic acid molecule for use as a primer, which molecule is selected from: Seq ID No 4, 5, 6, 7, 8, or 9.

16 A method of identifying and/or cloning the nucleic acid according to any one of claims 7 to 9, which method employs the nucleic acid molecule of any one of claims 11 to 15.

17 A method as claimed in claim 16 comprising the steps of:
(a) providing a preparation of nucleic acid,

(b) providing the nucleic acid molecule of any one of claims 11 to 15,
(c) contacting nucleic acid in said preparation with said nucleic acid molecule under conditions for hybridisation,
(d) identifying said SPASIC variant if present by its hybridisation with said nucleic acid molecule.

18 A method as claimed in claim 16 comprising the steps of:
(a) providing a preparation of nucleic acid,
(b) providing a pair of nucleic acid molecule primers suitable for PCR, at least one said primers being the nucleic acid molecule of any one of claims 12 to 15,
(c) contacting nucleic acid in said preparation with said primers under conditions for performance of PCR,
(d) performing PCR and determining the presence or absence of an amplified PCR product.

19 A method as claimed in claim 17 or claim 18 wherein the nucleic acid preparation is derived from dorsal root ganglia or spinal cord.

20 A method of producing a derivative nucleic acid acid according to claim 7 or claim 8, which method comprises the step of modifying a nucleic acid comprising Seq ID No 1.

21 A recombinant vector comprising the nucleic acid of ~~any one of~~ claim~~s~~ 5 ~~to 10~~.

22 A vector as claimed in claim 21 wherein the nucleic acid is operably linked to a promoter or other regulatory element for transcription in a host cell

23 A vector as claimed in claim 22 which is suitable for expression of the nucleic acid in a eucaryotic cell.

24 A host cell containing a heterologous nucleic acid of ~~any one of~~ claim~~s~~ 5 ~~to 10~~.

25 A host cell transformed with the vector of ~~any one of~~ claim~~s~~ 21 ~~to 23~~.

26 A host cell as claimed in claim 24 ~~or claim 25~~ which is selected from: a COS, CHO or HEK 293 cell or an oocyte.

27 A host cell comprising a heterologous protein of ~~any one of~~ claims 1 ~~to 4~~.

28 A method of influencing the electrophysiological and/or pharmacological properties of a cell, said method comprising the step of causing or allowing expression of a heterologous nucleic acid of ~~any one of~~ claim~~s~~ 5 ~~to 10~~ within the cell.

29 A method as claimed in claim 28 for increasing the ion channel activity in the cell.

30 A method as claimed in claim 28 for reducing the ion channel activity in the cell.

31 A method as claimed in claim 30 comprising the use of any of (i) all or part of the nucleic acid of claim 10 to reduce the activity by an anti-sense mechanism, (ii) part of the nucleic acid of any one of claims 5 to 9 to reduce activity by co-suppression, or (iii) use of a ribozyme specific for a nucleic acid of any one of claims 5 to 9.

32 A transgenic non-human mammal, comprising a cell of any one of claims 24 to 27 and/or a cell in which the electrophysiological and/or pharmacological properties has been altered in accordance with the method of any one

of claims 28 to 31.

33 A method for identifying a substance having ion-channel modulating activity, the method comprising the use of any of (i) the protein of any one of claims 1 to 4, (ii) a cell of any one of claims 24 to 27, (iii) a cell in which the electrophysiological and/or pharmacological properties has been altered in accordance with the method of any one of claims 28 to 31 (iv) the transgenic organism of claim 32.

34 A method as claimed in claim 33 comprising the steps of:
(i) exposing the protein of any one of claims 1 to 4, which is associated with a membrane or cell surface, to a solution of the substance such as to allow interaction between the substance and the protein,
(ii) measuring the electrophysiological response of the cell or membrane to this interaction.

35 A method as claim in claim 33 or claim 34 for screening for potential analgesics; neuromodulatory agents; anti-inflammatory agents; agents that regulate neurotransmitter release or neuronal excitability.

36 A method of influencing the electrophysiological and/or pharmacological properties of a cell, said method comprising the step of modulating the activity of the protein of ~~any one of~~ claims 1 ^ ~~to~~ 4.

37 A polypeptide comprising an antigen-binding site of an antibody capable of specifically binding the protein of ~~any one of~~ claims 1 ^ ~~to~~ 4.

38 Nucleic acid of any one of claims 5 to 10, or the vector of any one of claims 21 to 23, for use in gene therapy, or for use in the preparation of a medicament

for use in gene therapy.

39 The nucleic acid or vector of claim 39 wherein the therapy comprises the step of inhibiting a pain response and/or altering neurotransmitter release.